PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	01 NOV 2005
Applicant' s or agent's file reference 24028-015-06	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US05/10744	29 March 2005 (29.03.2005)	29 March 2004 (29.03.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12N 15/00; C12P 19/34 and US Cl.: 435/440, 91.1

Applicant

TABATADZE ET AL

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	19 September 2005 (19.09.2005)	Tara L. Garvey Telephone No. (571) 272-0507

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/10744

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☒ on paper

☒ in electronic form

c. time of filing/furnishing

☒ contained in the international application as filed.

☒ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/10744

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 26-40	YES
	Claims 1-5, 7-19, 21-25	NO
Inventive step (IS)	Claims 26-40	YES
	Claims 1-25	NO
Industrial applicability (IA)	Claims 1-40	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-5, 7-19 and 21-25 lack novelty under PCT Article 33(2) as being anticipated by anticipated by Pederson et al. Pederson et al teaches a method of site-directed alteration of an RNA molecule using an oligonucleotide that is flanked by nucleotide sequences unable to activate RNase H and a second oligonucleotide that is unmodified and hybridized to the moficied oligonucleotides and altering the RNA in the presence of Rnase. Furthermore, the alteration can be excision or excision and addition of nucleotides, the oligonucleotides can be modified with phosphorothioates, the flanking sequences can be modifies with methyl phosphonates. The method may be used to correst defects in an individual suffering from cystic fibrosis (abstract, column 1, lines 59-67, columns 2-6 and columns 11-12).

Claims 6 and 20 lack an inventive step under PCT Article 33(3) as being obvious over Pederson et al in view of Kole et al. Pederson et al does not specifically teach modifying the oligonucleotide by adding a 2-O-methyl moiety. Kole et al teaches modfying oligonucleotides with a 2-O-methyl moiety for alteration of RNA molecules (column 7, lines 44-67 and column 8, lines 1-7). In view of this teaching, it would have been obvious to one of ordinary skill in the art to modify the oligonucleotides with a 2-O-methyl moiety as described by Kole et al.

Claims 26-40 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method of repairing a gene by contacting an RNA molecule with a hybrid DNA/RNA oligonucleotide complex or an RNA oligonucleotide complex comprising SEQ ID NO:1 and SEQ ID NO:2.

Claims 1-40 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.